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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/499,006	02/04/00	BAGGOT	D 249/127

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HM12/1012

EXAMINER	
JOHANNSEN, D	
ART UNIT	**PAPER NUMBER**
1655	5

DATE MAILED: 10/12/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/499,006	Applicant(s) Baggot
	Examiner Diana Johannsen	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Jun 8, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 U.S.C. § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 are indefinite for failing to recite final process steps that clearly relate back to the claim preamble. Claims 1-5 are drawn to a method "of characterizing a chromosomal abnormality in a fetus by performing a comprehensive biochemical analysis of a specimen of amniotic fluid", claim 7 is drawn to a method "of performing a comprehensive biochemical analysis of a specimen of amniotic fluid in order to characterize a chromosomal abnormality in a fetus", and claims 8-11 are drawn to a method "of characterizing a chromosomal abnormality in a fetus by performing a comprehensive biochemical analysis of a specimen of amniotic fluid". Independent claims 1, 7 and 8 each recite a final process step of "prescribing a biochemical treatment". It is unclear as to how a step of "prescribing a biochemical treatment" might result in "characterization" of chromosomal abnormalities or "performing a comprehensive biochemical analysis". Accordingly, it is unclear as to whether the claims are intended to be drawn to methods

of "characterizing a chromosomal abnormality" or "performing a comprehensive biochemical analysis" or to methods for prescribing biochemical treatments. Clarification is required.

Claims 1-11 are indefinite over the recitation of the phrases "characterizing a chromosomal abnormality" and "generating a biochemical characterization" in claim 1, "characterize a chromosomal abnormality" and "generating a global biochemical characterization" in claim 7, and "characterizing a chromosomal abnormality" in claim 8. It is unclear as to what is intended to be encompassed by the terms "characterizing" and "characterization". For example, what actual information would have to be detected or gathered to accomplish "characterization" of a chromosomal abnormality, or to generate a biochemical or global biochemical "characterization"? As the meaning and scope of this language is unclear, the metes and bounds cannot be determined.

Claims 1-11 are indefinite over the recitation of the phrase "obtaining a comprehensive profile of metabolites". First, the scope of the language "comprehensive profile of metabolites" is unclear. The teachings of the specification and of the art do not provide a clear, limiting definition of this terminology, and it is unclear as to what amount of information regarding metabolites would be necessary in order for a profile to be considered "comprehensive". Second, it is unclear as to what is meant by the language "obtaining a comprehensive profile". Specifically, it is unclear as to whether this language is intended to require an actual active step of measuring levels of various metabolites, or whether this language might be intended to encompass, e.g., a step of reviewing published data regarding a particular sample. Clarification is required.

Claims 1-11 are indefinite over the recitation of the limitations "comprehensive biochemical analysis" and "analyzing the profile" in claims 1, 7, and 8, and "analyzed simultaneously" in claim 6. The term "analysis" and "analyzing" are vague and indefinite, as such language does not apprise one of skill in the art as to what actual steps must be taken to perform the claimed method. Further, these terms are sufficiently broad so as to encompass solely mental steps of "analysis". Accordingly, the claims should be amended so as to set forth active process steps.

Claims 1-11 are indefinite over the recitation of the limitation "identifying each metabolite" in claims 1, 7, and 8. The term "identifying" is vague and indefinite, as such language does not apprise one of skill in the art as to what actual steps must be taken to perform the claimed method. Further, the term "identifying" is sufficiently broad so as to encompass solely mental steps of "identification". Accordingly, the claims should be amended so as to set forth active process steps.

Claims 1-11 are indefinite over the recitation of the language "prescribing a biochemical treatment for each metabolite" in claims 1, 7, and 8. It is unclear as to what is meant by this language. Specifically, it is unclear as to whether this language is intended to suggest that a treatment is to be prescribed for, e.g., a fetus or a mother, or whether one is to actually "prescribe a treatment" for a "metabolite". Further, it is unclear as to what might be encompassed by the language "biochemical treatment". Clarification is required.

Claims 1-7 are indefinite over the recitation of the limitation "the normal profile" in claim 1, line 6 and claim 7, line 6. There is insufficient antecedent basis for this limitation in the claims, as the claims previously refer to a "control profile" but not to a "normal profile".

Claims 2-3 and 9-10 are indefinite over the recitation of the limitation "comparing the profile with respect to the normal profile". First, as the claims previously recite more than one type of "profile", it is unclear as to what is encompassed by the limitation "the profile" in claims 2-3 and 9-10. Second, as the claims previously recite steps of comparing a profile with a control profile, but not comparing a profile with a "normal profile", it is unclear as to how claims 2-3 and 9-10 are intended to further limit the claims from which they depend.

Claims 3 and 10 are indefinite over the recitation of the limitation "comparing..using nonparametric analysis". It is unclear as to what is meant by this language, as this language does not apprise one of skill in the art as to how "nonparametric analysis" is to be "used". Accordingly, the claims should be amended to recite active method steps.

Claim 4 is indefinite because it is unclear as to how the claim is intended to further limit claim 1, from which it depends. The claims is drawn to the method of claim 1 "wherein Down Syndrome is the chromosomal abnormality that is diagnosed". However, claim 1 is not drawn to a method of diagnosis, and does not require any steps of diagnosis. Accordingly, it is unclear as to whether claim 4 is intended to set forth an additional method step, to set forth a different method with a different objective, etc. Clarification is required.

Claim 5 is indefinite over the recitation of the limitation "the metabolite". While claim 1, from which claim 5 depends, refers to "metabolites", claim 5 does not refer to a particular "metabolite". Accordingly, there is insufficient antecedent basis in the claims for the limitation "the metabolite".

Claim 6 is indefinite because it is unclear as to how it is intended to further limit claim 1, from which it depends. The claim is drawn to the method of claim 1 "wherein the metabolites comprise multiple categories of metabolite groups that are analyzed simultaneously". It is unclear as to whether this recitation is intended to further limit the "analyzing" step of the method of claim 1, or whether this language is intended to set forth an additional step of simultaneous analysis. Clarification is required.

Claims 7 and 11 are indefinite over the recitation of the language "inferring an activity level for an enzyme that corresponds to" an identified metabolite and "inferring a cofactor level based on the activity level for the enzyme". First, it is unclear as to what active method step or steps might be encompassed by the language "inferring an activity" or "inferring a level based on" an activity level. Particularly, it is unclear as to whether the language "inferring" may be intended to encompass solely mental steps of, e.g., drawing an "inference". Second, it is unclear as to what relationship between an enzyme and a metabolite would be encompassed by the language "corresponds". Clarification is required.

Claims 8-11 are indefinite over the recitation of the limitation "the chromosomal abnormality profile" in claim 8. There is insufficient antecedent basis for this limitation in the

claims, as claim 8 previously refers to a "control profile" but not to a "chromosomal abnormality profile".

Claim Rejections - 35 U.S.C. § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-3 and 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffmann et al (Clin. Chem. 35(4):587-595 [4/1989]) in view of Galjaard (Ballieres Clin. Obst. Gyn. 1(3):547-567 [9/1987]).

Hoffmann et al teach a method "for qualitative and quantitative determination of organic acids, aldehydes, and ketones" in biological samples including urine, plasma, and amniotic fluid (see entire reference, especially p. 587). Hoffmann et al's method comprises steps of obtaining profiles of metabolites in a specimen, comparing profiles with normal control profiles and "analyzing" differences (see, e.g., Fig. 3, Tables 2-3). Further, Hoffmann et al suggest modifying treatments in response to metabolic profiles (p. 587). Hoffmann et al suggest that their method is intended to facilitate diagnosis and treatment of "acquired and inherited metabolic disorders" (p. 587), and teach that their method results in "quantitative multicomponent analysis of complex biological samples that is needed for the diagnosis and study of patients with new or ill-defined

disorders" (p. 594). However, Hoffmann et al do not specifically suggest employing their method to "characterize" or "analyze" a chromosomal abnormality in a fetus, as required by the instant claims. Galjaard discloses that one may diagnose a variety of genetic metabolic diseases in a fetus by "biochemical analysis of amniotic fluid supernatant" (see entire reference, especially p. 549-551). It is a property of such genetic diseases that they result from "chromosomal abnormality". In view of the teachings of Galjaard, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Hoffmann et al so as to have "analyzed" the metabolic profiles of individuals having or suspected of having a genetic disease in order to have identified known or unknown metabolic abnormalities associated with the disease and prescribed an appropriate treatment for such abnormalities. An ordinary artisan would have been motivated to have made such a modification for the advantage of rapidly detecting and treating metabolic abnormalities associated with a fetal chromosomal abnormality, as suggested by Hoffman et al and Galjaard. With respect to claims 2-3 and 9-10, it is further noted that Hoffmann et al exemplify comparing profiles by comparing means and standard deviations for metabolites (see, e.g., Tables 1-2, p. 592) and by comparing median levels using a nonparametric analysis (specifically, the Mann-Whitney rank sum test; see p. 592). With respect to claims 7 and 11, Galjaard discloses that one may "infer" enzyme and cofactor levels for enzymes that "correspond" to a metabolite (p. 551).

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday from 7:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at 703/308-1152. The fax phone number for the Technology Center where this application or proceeding is assigned is 703/305-3014 or 305-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana Johannsen

October 10, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

10/10/00